Diagnosis of Rheumatic Fever and Like Conditions

Evaluation of Certain of the Acute Phase Reactants in a Single Specimen of Blood

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• Certain of the acute phase reactant tests were performed on the same specimen of blood from persons with the following states: Normal, acute respiratory disease, streptococcosis, acute rheumatic fever, acute glomerulonephritis, acute rheumatoid arthritis, inactive rheumatic fever, lupus erythematosus, malignant disease, obesity, asthma, and allergic rhinitis. Of the tests performed, the mucoprotein-tyrosine and the antistreptolysin-0 titer when done together appeared to be the most discriminating. It is suggested that the performance of such tests on the same sample of blood might aid in differentiating mild acute rheumatic fever and acute rheumatoid arthritis from each other and also from other disease states.

MOST PHYSICIANS are readily able to diagnose acute rheumatic fever when it occurs in typical form. In these situations the criteria for establishing the diagnosis recommended by Jones[4] can be easily applied. It is quite likely, however, that in a significant number of patients the disease is not typically manifest and the criteria of Jones would not be sufficient to establish the diagnosis.

It is the author's opinion that in subtropical climates rheumatic fever infrequently occurs in typical form and is milder in its manifestations.[1] If some of the variations in the manifestations of the disease are represented as a spectrum, it might be stated that there is a shift to the left on the spectrum in the subtropical climates and a shift to the right in the temperate climates. Such a spectrum is illustrated in Chart 1.

It is in those clinical situations where the physician is considering the disease as occurring to the left of the spectrum and where the criteria of Jones are found wanting that special diagnostic aids are most helpful. It is the purpose of this paper to report the results of the performance of a battery of certain of the acute phase reactant tests on the same specimen of blood from patients with various disease states including rheumatic fever. Implications as to the value of such tests in differentiating mild rheumatic fever from other conditions will be discussed.

On each specimen of serum the following determinations were made: Mucoprotein-tyrosine, antistreptolysin-0 titer, C-reactive protein, and nonglucosamine polysaccharides. The methods and techniques used have been reported elsewhere.[3]

RESULTS

Normal Infants and Children

Table 1 summarizes the results obtained on the sera from the 76 normal infants and children. The average values were as follows: Mucoprotein-tyrosine, 3.3 mg. per 100 cc., ±0.5; antistreptolysin-0, 55 Todd units ±55; C-reactive protein, 0; nonglucosamine polysaccharides, 116 mg. per 100 cc. ±14.

Infants and Children with Various Diseases

Blood was obtained from 128 infants and children with the following various disease states: acute rheumatic fever, acute respiratory disease, streptococcosis, acute glomerulonephritis, acute rheumatoid arthritis, inactive rheumatic fever, lupus erythematosus, malignant disease, obesity, asthma and allergic rhinitis. In the cases of rheumatic fever, the diagnosis was based on the clinical findings and was not contingent upon the results obtained from the acute phase reactants. All the patients with acute glomerulonephritis had hypertension, hematuria, albuminuria and cylindruria. A number of the patients with inactive rheumatic fever were the same as those on whom values were obtained during the acute phase of the disease.

Table 2 contains a summary of the results obtained for the various values in the various disease states. From the data it was obvious that the main difference between acute respiratory disease and streptococcosis so far as these tests were concerned was the increased antistreptolysin titer in streptococcosis. In acute rheumatic fever, *all* the acute phase reactants were elevated and usually greatly so. The same was true of acute glomerulonephritis. In acute rheumatoid arthritis all the acute phase reactants are generally elevated except the anti-

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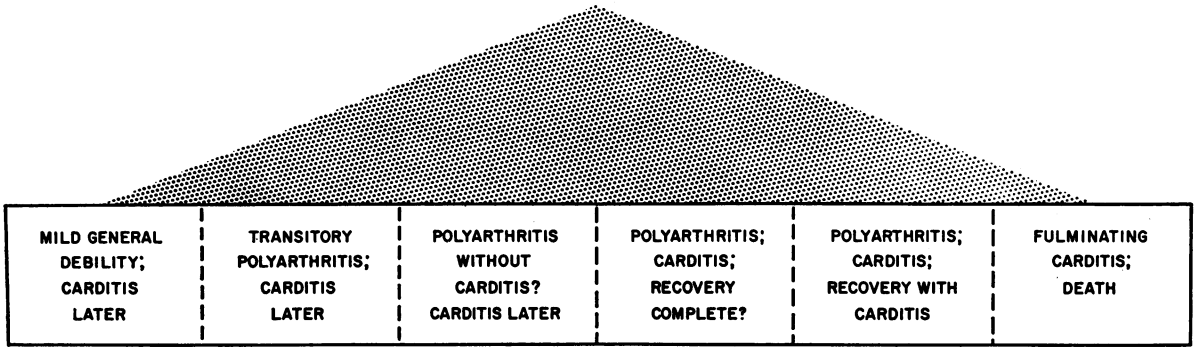

Chart 1.—Spectrum of manifestations of rheumatic fever.

TABLE 1.—*Values for Acute Phase Reactants Found in Apparently Healthy Children*

Determination	Number of Persons	Average	Measurement	Minimum	Maximum
Mucoprotein-tyrosine	76	3.3±0.5	mg. per 100 cc.	1.8	4.3
Antistreptolysin-0 titer	67	55±55	Todd Units	0	333
C-reactive protein	76	0	mm. of precipitation	0	2+
Nonglucosamine polysaccharides	75	116±14	mg. per 100 cc.	85	148

TABLE 2

Diagnosis	Number of Patients	Average Age (Years)	Average MPT	Average ASO	Average CRP	Average NGA
Lupus erythematosus	4	30	6.2	79	0	166
Malignant disease	6	7	7.6	258	4	187
Asthma	12	11	4.6	69	0	141
Allergic rhinitis	15	9	3.9	84	0	119
Obesity	14	13	4.1	86	0	138
Acute respiratory disease of probable nonbacterial origin	29	10	4.5	97	0	131
Streptococcosis	7	12	4.1	507	2	135
Acute rheumatic fever	15	9	7.4	533	3	180
Acute glomerulonephritis	7	8	6.4	314	2	184
Acute rheumatoid arthritis	6	5	9.5	10	4	208
Inactive rheumatic fever	13	10	3.1	98	0	121

Abbreviations: MPT=mucoprotein-tyrosine; ASO=antistreptolysin-0 titer; CRP=C-reactive protein; NGA=nonglucosamine polysaccharides.

streptolysin titer; why this is so is not apparent at present, but certainly this can be helpful in differentiating these two rheumatic diseases for which the prognosis is so different.

In general the acute phase reactant values were normal for the patients with asthma, allergic rhinitis and obesity. In lupus erythematosus the mucoprotein-tyrosine and the nonglucosamine polysaccharides were elevated but the antistreptolysin-0 titer was normal; the serum from only one patient contained C-reactive protein. In malignant disease all the values were regularly elevated except for the antistreptolysin-0 titer.

DISCUSSION

Unfortunately, one of the more commonly used acute phase reactants, the sedimentation rate, was not determined routinely during this study and its use is not reported here. Previous studies,[2,5,6] however, showed that sedimentation rate acceleration parallels quite closely the increased serum mucoproteins except in certain unusual situations, namely cardiac failure, nephrotic syndrome and in patients receiving steroid therapy.

The physiological significance of all the acute phase reactants except the antistreptolysin-0 titer still remains obscure. The antistreptolysin-0 titer, of course, is specific for hemolytic streptococcal infection, as it is a measure of the antibody response to the streptococcal antigen, streptolysin.

The author is aware that determinations on a single specimen of serum may not always be sufficient to establish the proper diagnosis. This is particularly true in differentiating prolonged uncomplicated streptococcal disease from mild rheu-

matic fever. In the former situation, all the acute phase reactants might be slightly to moderately elevated, but the duration of the elevation is the differentiating factor. In streptococcal disease the mucoprotein-tyrosine seldom remains elevated longer than 30 days. In patients with clear-cut evidence of rheumatic fever[6] it was found that the mucoprotein-tyrosine seldom returned to normal sooner than three months after the onset.

From the data presented, it would appear that the C-reactive protein is a substance only remotely related to the mucoprotein-tyrosine and the nonglucosamine polysaccharides. Many patients had elevated values for mucoprotein-tyrosine and nonglucosamine polysaccharides without evidence of C-reactive protein being present, and vice versa. As a result of this observation and certain clinical observations, in the author's experience it would appear that the results of the C-reactive protein determination are less predictable and therefore probably of less value.

The finding of essentially identical results of the acute phase reactants in the sera of patients with acute rheumatic fever and acute glomerulonephritis is not surprising. Epidemiologically, both diseases are thought to be related to infection by the beta hemolytic streptococcus, the main difference being that apparently only certain types of streptococci are nephrogenic whereas all types of streptococci are thought to be rheumatogenic. Too few observations have been made on patients with uncomplicated Sydenham's chorea to be included in this presentation but certainly a study of reactions in that disease should be done.

It was interesting to note that the major difference between the sera from patients with acute rheumatic fever and acute rheumatoid arthritis was the normal antistreptolysin-0 titer in the patients with rheumatoid arthritis. Although both diseases are generally classified as "collagen diseases," this difference suggests etiologic differences.

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REFERENCES

1. Adams, F. H.: Problems relating to the diagnosis of rheumatic fever in Southern California, Calif. Med., in press.

2. Adams, F. H., Kelley, V. C., Dwan, P. F., and Glick, D.: Response of the serum hyaluronidase inhibitor and mucoprotein to adrenocorticotropic hormone in rheumatic states, Pediatrics, 7:472, 1951.

3. Adams, F. H.: An appraisal of certain acute phase reactants in a single blood sample and their value in the diagnosis of acute rheumatic fever, J. Pediat., 49:16, 1956.

4. Jones, T. D.: The diagnosis of rheumatic fever, J.A.M.A., 126:481, 1944.

5. Kelley, V. C., Good, R. A., and McQuarrie, I.: Serum mucoproteins in children in health and disease with special reference to rheumatic fever, Pediat., 5:824, 1950.

6. Kelley, V. C., Adams, F. H., and Good, R. A.: Serum mucoproteins in patients with rheumatic fever, Pediat., 12:607, 1953.